

We claim:

1. A method of specifically inhibiting an immune response to one or more selected antigens comprising:
  - exposing purified or isolated antigen presenting cells (APCs) that present
  - 5 an antigen against which selective inhibition of an immune response is desired to an immunosuppressive composition comprising one or more factors secreted by a glioblastoma cell.
2. The method of claim 1, further comprising:
  - 10 introducing the purified or isolated APCs that have been exposed to the immunosuppressive composition into a subject in whom a reduced immune response to the antigen is desired, in a therapeutically effective amount sufficient to selectively inhibit the immune response of the subject to the antigen.
- 15 3. The method of claim 1, wherein the purified or isolated APCs are obtained from a transplant donor, and wherein the APCs express a transplant antigen against which specific inhibition of the immune response is desired.
4. The method of claim 1, wherein the APCs are obtained from a subject,
  - 20 wherein the APCs present an autoantigenic antigen against which specific inhibition of the immune response is desired.
5. The method of claim 4, wherein the purified or isolated APCs are incubated with an autoantigenic peptide, in an amount effective to cause the APCs
  - 25 to present the autoantigenic peptide.
6. The method of claim 1, wherein the method specifically inhibits the immune response by inducing apoptosis and/or anergy in T cells specific for the antigen.

7. The method of claim 2, wherein the APCs are obtained from a donor other than the subject, and the selected antigens are donor-specific antigens present on an allogenic graft.

5 8. The method of claim 7, wherein the APCs are obtained from a donor of an allogenic graft that is transplanted to the subject, and the introducing step comprises administering a sufficient dose of the exposed APCs to the subject to specifically inhibit the subject's immune response against an antigen presented by the APCs of the donor.

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9. The method of claim 1 wherein the antigen presented by the APCs is an autoantigenic protein of an autoimmune disease.

10. The method of claim 9, wherein the purified or isolated APCs are obtained  
15 from a subject suffering from an autoimmune disease, and the isolated or purified APCs are repetitively exposed to one or more peptide fragments of the autoantigenic protein of the autoimmune disease, and the introducing step comprises administering a therapeutically effective amount of the exposed APCs to the subject.

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11. The method of claim 10, wherein the autoimmune disease is selected from the group consisting of multiple sclerosis (MS), rheumatoid arthritis (RA), myasthenia gravis (MG), systemic lupus erythematosus (SLE), and insulin dependent diabetes mellitus (IDDM).

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12. The method of claim 10, wherein the autoantigenic protein is selected from the group consisting of myelin basic protein (MBP), type II collagen, acetyl choline receptor (AChR), nuclear proteins, and pancreatic islet cell antigens.

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13. The method of claim 1, wherein the APCs are selected from the group consisting of monocytes, macrophages, and dendritic cells.

14. The method of claim 13, wherein the APCs comprise monocytes.
15. The method of claim 8, wherein the APCs comprise monocytes isolated or  
5 purified from the donor's blood.
16. The method of claim 9, wherein the APCs comprise monocytes isolated or  
purified from the subject's blood.
- 10 17. The method of claim 1, wherein the glioblastoma cell is selected from the  
group consisting of SNB 19, U251 A172, A1207, A1235, A2781, U87 MG, U138  
MG and U373 MG.
18. A purified immunosuppressive composition for use in selectively reducing  
15 an immune response to one or more selected antigens in a subject, the composition  
comprising one or more factors secreted by a glioblastoma cell that have the  
following characteristics:
  - a) incubation of the composition with APCs presenting an antigen, and  
subsequent exposure of the incubated APCs to T cells specific for the antigen,  
20 induces the T cells to undergo anergy or apoptosis;
  - b) a molecular weight greater than about 40 kDa;
  - c) ability to bind to anion, but not cation exchange columns;
  - d) maintain an ability to induce T cells to undergo anergy or apoptosis  
under the conditions of a) within the pH range of 2 to 11, following heat exposure  
25 up to about 56° C, and following immunoprecipitation of TGF-  $\beta$ 1, TGF-  $\beta$ 2,  
TGF-  $\beta$ 3, IL-6, calcitonin gene related peptide (CGRP), and M-CSF from the  
composition; and
  - e) loses the ability to induce T cells to undergo anergy or apoptosis  
under the conditions of a) following heat exposure above 56° C, or after exposure  
30 to trypsin.

19. The immunosuppressive composition of claim 18, wherein incubation of the composition with an effective amount of monocytes, dendrites, and B cells causes effects comprising the following:

- 5 a) decreased expression of MHC class II antigens and CD 80/86 on the surface of the monocytes and the dendrites, but no effect on the expression of MHC class II antigens and CD 80/86 on the B cells;
- b) increased expression of IL-10 in monocytes and dendrites; and
- c) decreased the expression of IL-12 in monocytes and dendrites.

10 20. A method for enhancing tolerance in a host mammal to an allogenic donor graft, comprising:

exposing APCs obtained from a donor mammal to a therapeutically effective amount of a composition secreted by a glioblastoma cell, wherein the composition is effective to induce the APCs obtained from the donor mammal to  
15 secrete one or more factors that selectively inhibit clonal proliferation of a T cell that specifically recognizes an allogenic antigen presented by the APCs obtained from the donor mammal; and

administering a therapeutically effective dose of the APCs obtained from a donor mammal that have been exposed to the therapeutically effective amount of  
20 the composition secreted by the glioblastoma cell to the host mammal to inhibit recognition of the allogenic antigen by the host mammal by inhibiting the clonal proliferation of the T cell of the host mammal in response to presentation of the allogenic antigen by the APCs.

25 21. The method of claim 20, wherein the allogenic antigen is an antigen from the allogenic donor graft.

22. The method of claim 20, wherein obtaining the donor mammalian APCs comprises specifically isolating or purifying APCs that recognize the allogenic  
30 antigen in the donor graft.

23. The method of claim 22, wherein the APCs are obtained from a source selected from the group consisting of an organ, tissue, bone marrow and blood of the donor mammal.

5 24. A method for enhancing tolerance in a host mammal to an autoantigen, comprising:

obtaining APCs from the host mammal, wherein the APCs present an antigen to T cells which recognize the antigen and undergo a specific clonal proliferation to induce an immune response against the antigen;

10 culturing the APCs ex vivo in an effective amount of a composition secreted by a glioblastoma cell in an amount effective to induce the APCs to secrete one or more factors that selectively inhibit the specific clonal proliferation of the T cells that recognize the autoantigen presented by the APCs; and

administering a therapeutically sufficient dose of the APCs to the host  
15 mammal to inhibit recognition of the autoantigen by the host mammal.

25. The method of claim 2, wherein introducing the APCs into the subject comprises administering the APCs by a route selected from the group consisting of intravenous, subcutaneous, intramuscular, and intraperitoneal administration.

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26. The composition of claim 18 for use as a medicament.

27. The composition of claim 18 for use in a method of treating an immune mediated disease, comprising administering the composition to the subject.

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28. A method of inhibiting an immune response to one more selected antigens comprising contacting an APC with the composition of claim 18.

29. A method of making an immunosuppressive composition for use in  
30 suppressing an immune response to an antigen, comprising incubating a supernatant harvested from a glioblastoma cell culture and the antigen with an

APC, thereby producing an immunosuppressive composition that includes the APC.

30. The method of claim 29, further comprising combining the  
5 immunosuppressive composition with a pharmaceutical carrier.

31. The composition obtained by the method of claim 29.

32. The method of claim 29, further comprising purifying the APC to produce  
10 a substantially pure APC composition prior to incubating with the glioblastoma cell culture supernatant.

33. The method of claim 29, further comprising purifying the APC to produce  
15 a substantially pure APC composition after incubating with the glioblastoma cell culture supernatant.